

General

Guideline Title

The 2012 hormone therapy position statement of The North American Menopause Society.

Bibliographic Source(s)

The North American Menopause Society. The 2012 hormone therapy position statement of the North American Menopause Society. Menopause. 2012 Mar;19(3):257-71. [173 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: North American Menopause Society. Estrogen and progestogen use in postmenopausal women: 2010 position statement of The North American Menopause Society. Menopause 2010 Mar;17(2):242-55.

Recommendations

Major Recommendations

Conclusions and Recommendations

- Individualization is of key importance in the decision to use hormone therapy (HT) and should incorporate the woman's health and quality of life priorities as well as her personal risk factors, such as risk of venous thrombosis, coronary heart disease (CHD), stroke, and breast cancer.
- The recommendation for duration of therapy differs for combined estrogen-progestogen therapy (EPT) and estrogen therapy (ET). For EPT, duration is limited by the increased risk of breast cancer and breast cancer mortality associated with 3 to 5 years of use; for ET, a more favorable benefit-risk profile was observed during a mean of 7 years of use and 4 years of follow-up, a finding that allows more flexibility in duration of use.
- ET is the most effective treatment of symptoms of vulvar and vaginal atrophy; low-dose, local vaginal ET is advised when only vaginal symptoms are present.
- Women with premature or early menopause who are otherwise appropriate candidates for HT can use HT at least until the median age of natural menopause (age 51 years). Longer duration of treatment can be considered if needed for symptom management.
- Although ET did not increase breast cancer risk in the Women's Health Initiative (WHI), there is a lack of safety data supporting the use of ET in breast cancer survivors, and one randomized controlled trial (RCT) reported a higher increase in breast cancer recurrence rates.
- Both transdermal and low-dose oral estrogen have been associated with lower risks of venous thromboembolism (VTE) and stroke than standard doses of oral estrogen, but RCT evidence is not yet available.

Summary

In the decade since the first publication of results from the WHI EPT study, much has been learned. There is a growing body of evidence that HT formulation, route of administration, and the timing of therapy produce different effects. Constructing an individual benefit-risk profile is essential for every woman considering any HT regimen. A woman's interest in using HT will vary depending on her individual situation, particularly the severity of her menopausal symptoms and their effect on her quality of life. The absolute risks known to date for use of HT in healthy women ages 50 to 59 years are low. In contrast, long-term HT or HT initiation in older women is associated with greater risks.

Recommendations for duration of use differ between ET and EPT. Given the more favorable safety profile of ET, it could be considered for longer duration of therapy in the absence of adverse effects and risk factors. Women experiencing premature menopause are at increased risk of osteoporosis and, possibly, cardiovascular disease, and they often experience more intense symptoms than do women reaching menopause at the median age. Therefore, HT generally is advised for these young women until the median age of menopause when treatment should be reassessed.

Additional research is needed to understand the different effects of ET and EPT and how they apply to individual women. Further research is also needed to more clearly delineate the role of aging versus menopause and the effects of genetics, lifestyle, and individual clinical characteristics on midlife women's health.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Menopause-related symptoms
- Diseases occurring in postmenopausal women, including osteoporosis, cardiovascular disease (coronary heart disease, stroke, venous thromboembolism), diabetes mellitus, mood, depression, cognitive aging, and dementia

Guideline Category

Assessment of Therapeutic Effectiveness

Counseling

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Cardiology

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Neurology

Obstetrics and Gynecology

Oncology

Preventive Medicine

Psychiatry

Pulmonary Medicine

Urology

Intended Users

Advanced Practice Nurses

Health Care Providers

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To update the evidence-based position statement published by The North American Menopause Society (NAMS) in 2010 regarding recommendations for hormone therapy (HT) for postmenopausal women
- To clarify the benefit-risk ratio of estrogen therapy (ET) versus estrogen-progestogen therapy (EPT) for both treatment of menopause-related symptoms and disease prevention at various ages and time intervals since menopause onset

Target Population

Perimenopausal and postmenopausal women

Interventions and Practices Considered

1. Individualization of therapy according to woman's benefit-risk profile and differing effects of:
 - Hormone therapy (HT) formulation
 - Route of administration
 - Timing of therapy
2. Duration of use for estrogen therapy (ET) vs. estrogen-progestogen therapy (EPT)
3. ET for women with vulvar and vaginal atrophy
4. HT for women with premature or early menopause
5. Consideration of benefits associated with transdermal and low-dose oral estrogen administration

Major Outcomes Considered

Benefits and risks (including effectiveness, disease risks, and adverse effects) of peri- and postmenopausal estrogen therapy (ET) and estrogen-progestogen therapy (EPT) for both disease prevention and treatment of menopause-related symptoms, including:

- Vasomotor symptoms
- Vaginal symptoms
- Sexual function
- Urinary tract health

- Health-related quality of life
- Osteoporosis
- Cardiovascular effects, including coronary heart disease, stroke, and venous thromboembolism
- Diabetes mellitus
- Endometrial, breast, ovarian, and lung cancer
- Mood and depression
- Cognitive aging and dementia
- Premature menopause and primary ovarian insufficiency
- Total mortality

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A literature search was conducted in PubMed database through December 2011. No inclusion or exclusion criteria were used. Search terms included the following key words: bioidentical hormones, breast cancer, cardiovascular disease, cognitive decline, coronary heart disease, dementia, depression, diabetes mellitus, endometrial cancer, estrogen, estrogen progestogen therapy, estrogen therapy, hormone replacement therapy, hormone therapy, menopause, mood, The North American Menopause Society, osteoporosis, ovarian cancer, perimenopause, postmenopause, premature menopause, primary ovarian insufficiency, progestogen, sexual function, stroke, total mortality, urinary health, quality of life, vaginal atrophy, vaginal health, vasomotor symptoms, venous thromboembolism, Women's Health Initiative.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Description of Methods Used to Formulate the Recommendations

An Advisory Panel of clinicians and researchers expert in the field of women's health was enlisted to review the 2010 North American Menopause Society position statement, evaluate new evidence, and reach consensus on recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The position statement was reviewed and approved by the 2011–2012 North American Menopause Society (NAMS) Board of Trustees as an official NAMS position statement.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

- The type of evidence supporting the recommendations is not specifically stated.
- Because the Women's Health Initiative (WHI) is, for some outcomes, the only large long-term randomized controlled trial (RCT) of postmenopausal women using hormone therapy (HT), these findings were given prominent consideration among all the studies reviewed in the development of this position statement. In general, the panel gave more weight to RCTs.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate use of hormone therapy (HT) for treatment of menopause-related symptoms and prevention of disease
- Further distinguishing of the emerging differences in the therapeutic benefit-risk ratio between estrogen therapy (ET) and combined estrogen-progestogen therapy (EPT) at various ages and time intervals since menopause onset

Potential Harms

Increased risk or increased incidence of various diseases and conditions associated with estrogen therapy (ET) and/or estrogen-progestogen therapy (EPT):

- Endometrial hyperplasia

- Urinary stress incontinence
- Kidney stones
- Coronary heart disease (CHD)
- Ischemic stroke
- Venous thromboembolism (VTE)
- Endometrial cancer
- Breast cancer, breast cancer mortality and/or recurrence
- Breast cell proliferation, breast pain, mammographic density, and possible impedance of the diagnostic interpretation of mammograms, therein delaying the diagnosis of breast cancer
- Ovarian cancer
- Lung cancer
- Worsened mood
- Dementia incidence
- Uterine bleeding

Qualifying Statements

Qualifying Statements

- The North American Menopause Society acknowledges that no single trial data can be extrapolated to all women. However, because the Women's Health Initiative (WHI) is, for some outcomes, the only large long-term randomized controlled trial (RCT) of postmenopausal women using hormone therapy (HT), these findings were given prominent consideration among all the studies reviewed in the development of this position statement. Nonetheless, the WHI hormone trials had several characteristics that limit generalizing the findings to all postmenopausal women. These include the use of only one route of administration (oral), only one formulation of estrogen (conjugated estrogens [CEs]), and only one progestogen (medroxyprogesterone acetate). Unlike most HT studies that focused on symptomatic, recently postmenopausal women, the WHI enrolled generally healthy postmenopausal women aged 50 to 79 years in a prevention trial. These parameters should be taken into consideration when applying the WHI findings to clinical practice as should be the findings from observational studies with their known limitations. In general, the panel gave more weight to RCTs.
- These statements do not represent codified practice standards as defined by regulating bodies and insurance agencies.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2002 Oct 6 (revised 2012 Mar)

Guideline Developer(s)

The North American Menopause Society - Nonprofit Organization

Source(s) of Funding

The North American Menopause Society (NAMS)

Guideline Committee

The North American Menopause Society (NAMS) 2012 Hormone Therapy Position Statement Advisory Panel

Composition of Group That Authored the Guideline

Advisory Panel Members: Margery L.S. Gass, MD, NCMP (*Co-Chair*); JoAnn E. Manson, MD, DrPH, NCMP (*Co-Chair*); Felicia Cosman, MD; Francine Grodstein, ScD; V. Craig Jordan, OBE, PhD, DSc, FMedSci; Richard H. Karas, MD, PhD; Andrew M. Kaunitz, MD; Pauline M. Maki, PhD; Peter J. Schmidt, MD; Jan L. Shifren, MD, NCMP; Cynthia A. Stuenkel, MD, NCMP; and Wulf H. Utian, MD, PhD, DSc (Med), NCMP

Financial Disclosures/Conflicts of Interest

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For the Advisory Panel, Dr. Cosman reports: Consultant/Advisory Board: Amgen, Eli Lilly, Merck, Novartis, Zosano; Grants/Research Support: Eli Lilly, Novartis; Speaker's Bureau: Amgen, Eli Lilly, Novartis; Dr. Gass reports: No significant financial relationships. Dr. Grodstein reports: No significant financial relationships. Dr. Jordan reports: No significant financial relationships. Dr. Karas reports: No significant financial relationships. Dr. Kaunitz reports: Consultant/Advisory Board: Bayer, Merck, Noven, Teva; Grants/Research Support: Bayer, Endoceutics, Medical Diagnostic Laboratories, Merck, Noven, Teva. Dr. Maki reports: Consultant/Advisory Board: Noven. Dr. Manson reports: No significant financial relationships. Dr. Schmidt reports: No significant financial relationships. Dr. Shifren reports: Consultant/Advisory Board: New England Research Institutes; Grants/Research Support: Boehringer Ingelheim. Dr. Stuenkel reports: Consultant/Advisory Board: Noven, Pharmavite. Dr. Utian reports: Consultant/Advisory Board: Bayer, Bionovo, Cleveland Clinic Foundation Innovations Center, Hygeia (Orcas Therapeutics), Lupin, Merck, Novogyne, Pharmavite.

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For the NAMS Board of Trustees, Dr. Clarkson reports: Consultant/Advisory Board: Pfizer; Grants/Research Support: Merck, Pfizer. Dr. Gass reports: No significant financial relationships. Dr. Goldstein reports: Board of Directors/Trustees: New York University (NYU) School of Medicine Alumni Corporation (President-Elect), American Institute of Ultrasound in Medicine, SonoSite (President); Consultant/Advisory Board: Amgen, Bayer, Cook Ob/Gyn, Philips, Ultrasound, Shionogi; Speaker's Bureau: Amgen, Warner Chilcott. Dr. Kagan reports: Consultant/Advisory Board: Amgen, Bionovo, Depomed, Foundation for Osteoporosis Research and Education/American Bone Health, Merck, Novo Nordisk, Own the Bone Advisory Board of the American Orthopedic Association, Pfizer, Shionogi; Grants/Research Support: Boehringer Ingelheim, Bionovo, Biosante, Depomed, Pfizer; Speaker's Bureau: Amgen, Novogyne, Novo Nordisk. Dr. Kaunitz reports: Consultant/Advisory Board: Bayer, Merck, Noven, Teva; Grants/Research Support: Bayer, Endoceutics, Medical Diagnostic Laboratories, Merck, Noven, Teva. Dr. Maki reports: Consultant/Advisory Board: Noven. Dr. Manson reports: No significant financial relationships. Dr. Pace reports: Consultant/Advisory Board: Novo Nordisk; Speaker's Bureau: Novo Nordisk. Dr. Schiff reports: No significant financial relationships. Dr. Schnatz reports: Board of Directors/Trustees: FaithCare. Dr. Shapiro reports: Board of Directors/Trustees: Baycrest, Research Canada, Canadian Partnership Against Cancer, SIGMA Canadian Menopause Society; Employment: Consultant, CTV Canada AM, CTV National News, CTV NewsChannel, Parents Canada, Canadian Health Consultant/Advisory Board: Amgen, AstraZeneca, Novartis, Pfizer; Grants/Research Support: Amgen, Pfizer, SIGMA; Speaker's Bureau: Amgen, AstraZeneca, Bayer, GlaxoSmithKline, Merck, Novartis, Novo Nordisk, Pfizer, Sanofi Pasteur, Warner Chilcott; Website Writer: CTV.ca. Dr. Shifren reports: Consultant/Advisory Board: New England Research Institutes; Grants/Research Support: Boehringer Ingelheim. Dr. Sievert reports: No significant financial relationships. Dr. Utian reports: Consultant/Advisory Board: Bayer, Bionovo, Cleveland Clinic Foundation Innovations Center, Hygeia (Orcas Therapeutics), Lupin, Merck, Novogyne, Pharmavite. Dr. Warren reports: Consultant/Advisory Board: Pfizer, Yoplait; Grants/Research Support: Pfizer; Speaker's Bureau: Amgen, Ascend Therapeutics, Pfizer, Upsher Smith

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Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from [The North American Menopause Society \(NAMS\) Web site](#)

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Availability of Companion Documents

The following is available:

- NAMS 2012 position statement on hormone therapy. Slide set. 2012. Available to registered members from [The North American Menopause Society \(NAMS\) Web site](#) .

Patient Resources

The following is available:

- Hormone therapy for women in 2012. Patient handout. Mayfield Heights (OH): North American Menopause Society; 2012. 2 p. Electronic copies: Available in Portable Document Format (PDF) from [The North American Menopause Society \(NAMS\) Web site](#)

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This NGC summary was completed by ECRI on January 23, 2003. The information was verified by the guideline developer on February 13, 2003. This summary was updated by ECRI on March 5, 2004. The information was verified by the guideline developer on March 29, 2004. This NGC summary was updated by ECRI Institute on May 4, 2007. The updated information was verified by the guideline developer on May 9, 2007. This NGC summary was updated by ECRI Institute on October 9, 2008. The updated information was verified by the guideline developer on October 17, 2008. This summary was updated by ECRI Institute on June 30, 2010. The information was verified by the guideline developer on July 29, 2010. This NGC summary was updated by ECRI Institute on April 12, 2012. The updated information was verified by the guideline developer on April 19, 2012.

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